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Measurement of aortic regurgitation by Doppler echocardiography

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SUMMARY In an attempt to develop a new approach to the non-invasive measurement of aortic regurgitation, transmitral volumetric flow (MF) and left ventricular total stroke volume (SV) were measured by Doppler and cross sectional echocardiography in 23 patients without aortic valve disease (group A) and in 26 patients with aortic regurgitation (group B). The transmitral volumetric flow was obtained by multiplying the corrected mitral orifice area by the diastolic velocity integral, and the left ventricular total stroke volume was derived by subtracting the left ventricular end systolic volume from the end diastolic volume. The aortic regurgitant fraction (RF) was calculated as: $RF = 1 - MF/SV$. In group A there was a close agreement between the transmitral volumetric flow and the left ventricular total stroke volume, and the difference between the two measurements did not differ significantly from zero. In group B the left ventricular total stroke volume was significantly larger than the transmitral volumetric flow, and there was good agreement between the regurgitant fractions determined by Doppler echocardiography and radionuclide ventriculography. Discrepancies between the two techniques were found in patients with combined aortic and mitral regurgitation or a low angiographic left ventricular ejection fraction ($<35\%$). The effective cardiac output measured by Doppler echocardiography accorded well with that measured by the Fick method.

Doppler echocardiography provides a new and promising approach to the non-invasive measurement of aortic regurgitation.

The importance of measuring aortic regurgitation has been recognised for more than 150 years,[1] but a suitable technique is still lacking. Invasive techniques have limitations which preclude their use in serial evaluation.[2 3] Among the non-invasive techniques, radionuclide ventriculography has proved to be an accurate method for measuring aortic regurgitation but has the disadvantages of high cost and of requiring exposure to radiation.[4 5] Recently, Doppler echocardiography has been used to assess aortic regurgitation, but the proposed approaches are still semiquantitative.[6–8]

The regurgitant volume must be known before aortic regurgitation can be assessed.[9] It is now possible to measure the transmitral volumetric flow by Doppler echocardiography[10–12] and the left ventricular total stroke volume by cross sectional echocardiography.[13–15] Theoretically, the two volume measurements should be equal when the left ventricular diastolic inflow comes solely through the mitral orifice. If, however, the left ventricular diastolic inflow comes through both the aortic and mitral valves, as in aortic regurgitation, the two measurements will differ with the difference being equal to the aortic regurgitant volume. The present study was undertaken to test this assumption in patients with a normal aortic valve and in those with aortic regurgitation. We compared results obtained by Doppler echocardiography with those obtained by radionuclide ventriculography and cardiac catheterisation.

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Table 1 *Results of Doppler echocardiography in group A*

Case	*Diagnosis*	*CMA (cm^2)*	*DVI (cm)*	*MF (cm^3)*	*EDV (cm^3)*	*ESV (cm^3)*	*SV (cm^3)*	*RF (%)*
1	CCM + MR	2·99	15·7	47	261	218	43	−9·3
2	CAD	3·67	18·5	68	339	267	72	5·6
3	PE	4·18	17·4	73	177	105	72	−1·4
4	CAD	5·13	16·9	87	224	128	96	9·4
5	CAD	3·96	18·9	75	130	58	72	−4·2
6	N	3·69	18·8	69	221	140	81	14·8
7	CAD	4·86	14·4	70	129	69	60	−16·7
8	N	5·62	11·8	66	123	53	70	5·7
9	CAD	5·27	17·1	90	209	127	82	−9·8
10	N	4·26	24·7	105	204	106	98	−7·1
11	CAD	3·35	20·8	70	334	267	67	−4·5
12	PS	4·78	23·5	112	194	86	108	−3·7
13	HCM	5·20	16·4	85	179	94	85	0
14	CAD	4·76	18·2	87	410	320	90	3·3
15	N	4·60	17·6	81	109	33	76	−6·6
16	MR	6·12	19·6	120	235	104	131	8·4
17	AVR	4·05	19·4	79	216	124	92	14·1
18	N	4·37	23·0	100	170	70	100	0
19	PE	6·89	15·1	104	159	65	94	−10·6
20	N	5·48	24·0	132	222	91	131	−1·0
21	PS	4·66	18·7	87	144	62	82	−6·1
Mean (SD)		4·66	18·6	86	209	123	86	−0·92
		(0·93)	(3·3)	(20)	(77)	(79)	(21)	(8·3)

CMA, corrected mitral orifice area; DVI, diastolic velocity integral; MF, transmitral volumetric flow; EDV, left ventricular end diastolic volume; ESV, left ventricular end systolic volume; SV, left ventricular total stroke volume; RF, aortic regurgitant fraction; CCM, congestive cardiomyopathy; MR, mitral regurgitation; CAD, coronary artery disease; N, normal; PE, pericardial effusion; PS, pulmonary stenosis; HCM, hypertrophic cardiomyopathy; AVR, prosthetic aortic valve replacement.

Patients and methods

PATIENTS

Forty nine patients who underwent diagnostic cardiac catheterisation gave their informed consent to the study. They were divided into two groups according to clinical and angiographic findings. Group A consisted of 23 patients (17 men and six women, ranging in age from 17 to 65 years, mean 57) without evidence of aortic valve disease. Group B consisted of 26 patients (18 men and eight women, ranging in age from 17 to 76 years, mean 52) with aortic regurgitation. Tables 1 and 2 give the clinical diagnoses in both groups. None of these patients had mitral stenosis and all had a normal left ventricular wall motion except for a few cases with a generalised left ventricular hypokinesia. In group B, 14 patients had pure aortic regurgitation and 12 had concomitant valve lesions. The angiographic left ventricular ejection fraction was normal ($\geqslant 50\%$) in 22 patients and significantly reduced ($\leqslant 35\%$) in four. All patients were in sinus rhythm. Doppler echocardiography, radionuclide ventriculography, and cardiac catheterisation were performed independently by different investigators and the results were not compared until after the study was completed.

DOPPLER ECHOCARDIOGRAPHY

Transmitral volumetric flow and left ventricular total stroke volume were measured independently by two different investigators. A phased array sector scanner (IREX III) with a wide scanning angle of 80° and a 2·5 MHz transducer was used for echocardiographic recordings. A multifrequency (1–10 MHz) Doppler instrument (ALFRED, Vingmed) with both continuous and pulsed modes and a 2 MHz transducer were used for velocity measurement. In the pulsed mode the sample volume is about 8 mm in diameter and 5 mm in length. The received signals were processed by two frequency estimators and converted into analogue voltage in proportion to the mean and maximum Doppler frequency shifts. A direct audio output aided the identification of the best transducer position. Calculations were performed by means of a graph pen microcomputer system (CARDIO 80, Kontron).

MEASUREMENT OF THE TRANSMITRAL VOLUMETRIC FLOW

Transmitral volumetric flow was measured by our previously described technique.[11] The maximal mitral orifice area in early diastole was measured by cross sectional echocardiography from the left parasternal short axis view. A derived M mode echocardiogram of the mitral valve was digitised to obtain the mitral orifice opening ratio.[11] The corrected mitral orifice area (CMA) was calculated by multiplying the maximum mitral orifice area by the opening ratio. The Doppler transducer was placed at the apex and the fastest velocities of the transmitral flow were recorded with the pulsed mode at a position where the mitral valve opening was clearly

Table 2 *Results of Doppler echocardiography in group B*

Case	*Diagnosis*	*CMA (cm^2)*	*DVI (cm)*	*MF (cm^3)*	*EDV (cm^3)*	*ESV (cm^3)*	*SV (cm^3)*	*RF (%)*
1	AR + AS	3·62	21·6	78	241	72	169	54
2	AR	3·26	22·7	74	377	169	208	64
3	AR	5·46	21·6	118	483	188	295	60
4	AR + MR	3·67	35·6	131	408	143	265	51
5	AR	1·75	43·7	76	371	176	195	61
6	AR	4·84	18·8	91	412	182	230	60
7	AR	2·89	21·6	62	168	86	82	24
8	AR	6·28	14·9	94	342	193	149	37
9	AR	3·81	22·5	86	264	114	150	43
10	AR	2·41	22·4	54	246	127	119	55
11	AR + AS + MR	5·23	21·2	111	276	97	179	38
12	AR + AS	4·44	19·6	87	272	127	145	40
13	AR + AS + MR + TR	2·25	33·8	76	360	253	107	29
14	AR + MR	3·38	14·2	48	274	189	85	44
15	AR	4·24	22·0	93	423	203	220	58
16	AR	3·44	19·9	68	296	130	166	59
17	AR + AS	3·27	20·4	67	215	140	75	11
18	AR	3·33	27·4	91	294	123	171	47
19	AR + MR	4·05	25·5	103	334	160	174	41
20	AR + AS	4·02	25·7	103	344	137	207	50
21	AR	3·26	27·8	90	486	200	286	68
22	AR + AS	3·57	21·2	76	149	46	103	26
23	AR + AS	3·44	23·9	82	211	88	123	33
24	AR	5·23	17·6	92	199	83	116	21
25	AR	3·32	15·9	53	279	219	60	12
Mean (SD)		3·78 (1·04)	23·3 (6·6)	84 (20)	309 (91)	145 (51)	163 (65)	43 (16)

AR, aortic regurgitation; AS, aortic stenosis; TR, tricuspid regurgitation. See Table 1 for other abbreviations.

heard. In cases with severe aortic regurgitation and mitral valve fluttering the velocities were measured 1 cm above the level of the mitral valve opening. Care was taken to avoid the regurgitant jet and to reduce the effect of the mitral valve fluttering while still measuring the fastest transmitral flow. The maximal velocity curves of the mitral flow were integrated to obtain the diastolic velocity integral (DVI). Assuming that the angle between the Doppler beam and the mitral flow is zero, the transmitral volumetric flow (MF) was calculated as: $MF = CMA \times DVI$. The effective cardiac output (CO) in the presence of aortic regurgitation in group B was calculated as: $CO = MF \times HR$, where HR is the heart rate during Doppler study. At least six beats were averaged to obtain all the variables.

MEASUREMENT OF LEFT VENTRICULAR TOTAL STROKE VOLUME

With the transducer at the apex the apical four chamber view was recorded by cross sectional echocardiography focusing on the left ventricle. To avoid foreshortening of the left ventricle the transducer was moved along in three spatial directions—that is caudally and cranially to reach the most apical position, dorsally and ventrally to image the maximum left ventricular long axis, and medially and laterally to obtain the maximum short axis. All images were recorded on video tapes. The frames with the largest and smallest left ventricular cavity size within one cardiac cycle were selected to calculate the end diastolic and end systolic volume respectively. The inner edges of the endocardial echoes were traced and if there was echo dropout a straight line was drawn between the two adjacent echoes. The programme used for volume (V) computation is based on the area-length method[16] as: $V = 8A^2/3\pi L$, where A is the area of the left ventricular cavity and L is the left ventricular long axis which was taken as running from the junction of the septum and the mitral valve to the apex. The left ventricular total stroke volume (SV) was then calculated as: $SV = EDV - ESV$, where EDV is the left ventricular end diastolic volume and ESV is the end systolic volume. Five to seven beats were digitised and the values were averaged.

Theoretically, in patients without aortic regurgitation the transmitral volumetric flow (MF) should equal left ventricular total stroke volume (SV). In patients with aortic regurgitation the difference between the two measurements should equal the aortic regurgitant volume. The aortic regurgitant fraction (RF) was thus calculated in both groups as: $RF = 1 - MF/SV$.

RADIONUCLIDE VENTRICULOGRAPHY

Gated blood pool imaging was performed within 24 hours of Doppler echocardiography in group B by means of a GE scintillation camera (400 T AZS) interfaced to a GE STAR computer system. Erythrocytes were labelled by a combined in vivo and in vitro method. With the patient in a supine position the detector was located in the 40° left anterior projection with 15° caudal tilt to optimise a four chamber view. Under the STAR computer's PAGE multigated cardiac protocol 300 heart beats were stored in frame mode. Both left and right ventricular activity curves were analysed by an identical automatic technique including phase analysis for variable regions of interest and background area selection. In some cases operator intervention was necessary to achieve separation of the images of the right ventricle and right atrium. Separate regions of interest for end diastole and end systole were used to calculate ventricular stroke counts. The aortic regurgitant fraction (RF) was calculated as: $RF = 1 - RVSC/LVSC$, where RVSC is the right ventricular stroke count and LVSC the left ventricular stroke count. Because the mean left to right ventricular stroke count ratio in patients without valvar heart disease is 1·12 in this laboratory, the regurgitant fraction was corrected by multiplying the right ventricular stroke count by 1·12.

CARDIAC CATHETERISATION

All patients underwent left heart catheterisation. In addition, right heart catheterisation was performed 24 hours before or 24 hours after Doppler echocardiography in 23 patients in group B. Cardiac output was measured according to the Fick method.

STATISTICAL ANALYSIS

Methods were compared by the statistical method of Altman and Bland[17] and by paired and unpaired *t* tests. Data were expressed as mean (1 SD).

Results

DOPPLER ECHOCARDIOGRAPHY

Technically adequate Doppler echocardiographic recordings were obtained in 21 (91%) patients in group A and in 25 (96%) patients in group B. Two patients in group A were excluded because of suboptimal echocardiographic images and one patient in group B was excluded due to unsatisfactory Doppler velocity recordings. Tables 1 and 2 list the individual results in the remaining 21 patients in group A and 25 patients in group B. In group A the transmitral volumetric flow ranged from 47 to 132 cm^3 (86 (20) cm^3) and the left ventricular total stroke volume from 43 to 131 cm^3 (86 (21) cm^3). In group B the transmitral volumetric flow ranged from 48 to 131 cm^3 (84 (20) cm^3) and the left ventricular total stroke volume from 60 to 295 cm^3 (163 (65) cm^3).

RADIONUCLIDE VENTRICULOGRAPHY

Technically adequate radionuclide images were obtained in 25 (96%) patients in group B while one patient was excluded because of unsatisfactory separation of the right ventricle from the right atrium. In the 25 patients the left ventricular ejection fraction ranged from 26% to 74% (57 (15)%) and the right ventricular ejection fraction from 23% to 62% (46 (11)%). Mean aortic regurgitant fraction was 44% (19) (range 0%–67%). In two cases (17 and 25) in group B regurgitant fraction was zero and the angiographic left ventricular ejection fraction was low (<35%).

COMPARISON BETWEEN TRANSMITRAL VOLUMETRIC FLOW AND LEFT VENTRICULAR TOTAL STROKE VOLUME

In group A there was a close agreement between the two measurements. The difference between the two measurements did not correlate with the mean of the two measurements and did not differ significantly from zero (Fig. 1). The relative bias calculated from the mean difference between the two measurements was 0·24 cm^3 and the estimate of error calculated from the standard deviation of these differences was 6·96 cm^3. The agreement between the two measurements was not affected by mitral regurgitation

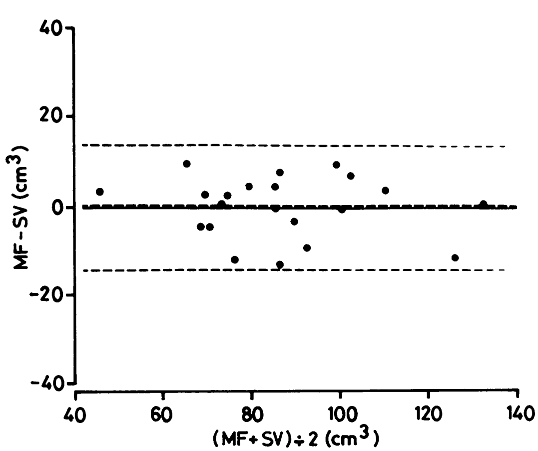

Fig. 1 *Difference between the transmitral volumetric flow and the left ventricular total stroke volume (MF − SV) is plotted against the mean of the two measurements (MF + SV) ÷ 2) in group A. Broken lines indicate the mean and the 95% range of the differences between the two measurements. This type of plot allows an easier and better assessment of the difference between two methods than conventional correlation and regression analysis.[17] The difference between methods (MF − SV) is independent of the size of measurement (MF + SV) ÷ 2) and does not differ significantly from zero. The relative bias and the estimate of error are 0·24 cm³ and 6·96 cm³ respectively.*

present in two cases (1 and 16) in group A. The aortic regurgitant fraction was −0·92% (8·3)% (range −16·7%–14·1%). In group B the left ventricular total stroke volume was larger than the transmitral volumetric flow in all cases and there was a significant difference between the two measurements (163 (65) cm^3 *vs* 84 (20) cm^3, $p<0·001$). The aortic regurgitant fraction was 43 (16)% (range 11%–68%).

COMPARISON BETWEEN DOPPLER ECHOCARDIOGRAPHY AND RADIONUCLIDE VENTRICULOGRAPHY

The results of Doppler echocardiography were compared with those of radionuclide ventriculography in 24 patients in group B in whom both recordings were adequate. The difference between the regurgitant fractions determined by Doppler and radionuclide techniques did not correlate with the mean of the two measurements and did not differ significantly from zero (Fig. 2). The relative bias was 0·21% and the estimate of error was 10·5%. In five patients with combined aortic and mitral regurgitation (two of whom also had an angiographic left ventricular ejection fraction <35%) the regurgitant fractions by radionuclide technique were considerably higher than those derived from Doppler echocardiography. When these five patients were excluded, there was a good agreement between the two measurements, with the relative bias and the estimate of error being 3·5% and 6·4% respectively. The results obtained by the two techniques differed in the two patients with a low angiographic left ventricular ejection fraction (<35%) in whom the regurgitant fraction by radionuclide ventriculography was zero, but concomitant aortic stenosis did not adversely affect the agreement between results obtained by the two techniques.

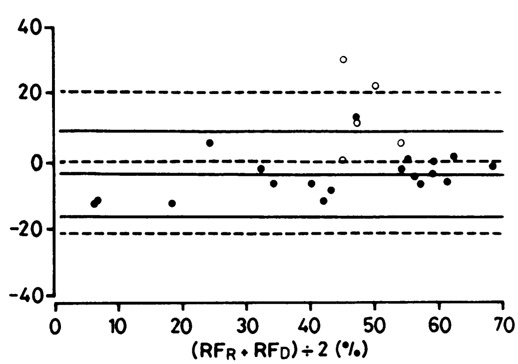

Fig. 2 *Difference between the regurgitant fractions determined by radionuclide and Doppler techniques ($RF_R - RF_D$) vs the mean of the two measurements (($RF_R + RF_D$) ÷ 2) in group B. The broken lines show the mean and the 95% range of the differences between the two measurements in the whole group. The solid lines show the mean and the 95% range of the differences between the two measurements in patients without mitral regurgitation. The difference between methods ($RF_R - RF_D$) is independent of the size of measurement (($RF_R + RF_D$) ÷ 2) and does not differ significantly from zero. The relative bias and the estimate of error are 0·21% and 10·5% in the whole group and 3·5% and 6·4% in patients without mitral regurgitation respectively. Closed circles, aortic regurgitation; open circles, aortic and mitral regurgitation.*

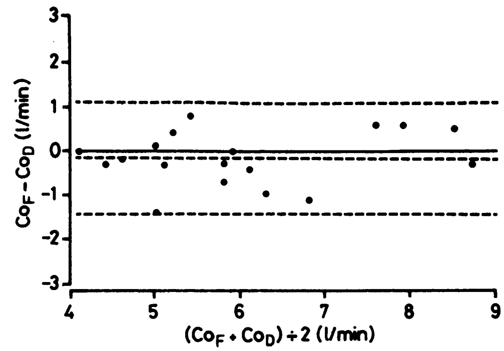

Fig. 3 *Difference between the effective cardiac output measured by Doppler echocardiography and Fick method ($Co_F - Co_D$) vs the mean of the two measurements (($Co_F + Co_D$) ÷ 2 in group B. Broken lines indicate the mean and the 95% range of the differences between the two measurements. The difference between methods ($Co_F - Co_D$) is independent of the size of measurement (($Co_F + Co_D$) ÷ 2) and does not differ significantly from zero. The relative bias and the estimate of error are 0·16 l/min and 0·62 l/min respectively.*

COMPARISON BETWEEN DOPPLER ECHOCARDIOGRAPHY AND CARDIAC CATHETERISATION

The effective cardiac output determined by Doppler echocardiography was compared with that obtained by the Fick method in 18 patients in group B without mitral regurgitation who underwent right heart catheterisation. There was a good agreement between the two techniques. The difference between the two measurements did not correlate with the mean of the two measurements and did not differ significantly from zero (Fig. 3). The relative bias and the estimate of error were 0·16 l/min and 0·62 l/min respectively.

Discussion

The size of the aortic regurgitant volume depends on the cross sectional area of the valve defect, the diastolic pressure gradient across the aortic valve, and the duration of diastole.[9] Although Doppler echocardiography has been used to estimate these determinants, direct measurement of the regurgitant volume has proved difficult.[6-8] In the present study the aortic regurgitant volume was calculated as the difference between the left ventricular total stroke volume as measured by cross sectional echocardiography and the transmitral volumetric flow measured by Doppler technique. The accuracy of this method is dependent upon that of the two combined measurements. The transmitral volumetric flow measurement by Doppler echocardiography has been validated by us and other workers against established invasive techniques.[10-12] As a result of aortic regurgitation the mitral orifice area in group B tended to be smaller than that in group A, resulting in an increased diastolic velocity integral. All of our patients, however, had a maximal mitral orifice area larger than that in mitral stenosis ($<2\cdot5\ cm^2$).[18] Although both the regurgitant jet and the transmitral flow come towards the transducer during diastole, differences in the quality of audio signals, the timing of flow velocities, and the position of sample volumes make the distinction between the two flows relatively easy. The effect of mitral valve fluttering can be minimised by adjusting the position of the sample volume in the mitral flow canal, since small changes in sample volume position do not significantly affect the transmitral volumetric flow measurement.[11] The good agreement between the effective cardiac output determined by Doppler echocardiography and the Fick method demonstrates that the transmitral volumetric measurement is still valid even in the presence of aortic regurgitation.

Measurement of the left ventricular volume by cross sectional echocardiography has proved reasonably accurate in the absence of regional left ventricular wall dyskinesia.[13-15] Because the four chamber view can be easily obtained in most adult patients, we used this view and the area-length formula to calculate the left ventricular volume. The fact that a known left ventricular volume is consistently overestimated by the area-length formula in angiography,[19 20] while it is often underestimated by the same formula in echocardiography,[21] indicates that the most important pitfall in volume measurement by cross sectional echocardiography is the foreshortening of the left ventricle rather than the geometric assumption.[22] Therefore, we made great efforts to avoid foreshortening of the left ventricle in this study. The good results obtained in the study indicate that left ventricular total stroke volume can be reliably estimated by cross sectional echocardiography.

Combining the transmitral volumetric flow and the left ventricular total stroke volume measurements offers several advantages for determining the regurgitant volume. Firstly, use of cross sectional echocardiography to measure the left ventricular total stroke volume avoids the difficulties in determining the aortic volumetric flow by Doppler technique in patients with a dilatated ascending aorta.[23] Secondly, the volume measurement by cross sectional echocardiography is not affected by the concomitant aortic stenosis, where the aortic volumetric flow measurement becomes invalid.[23] Thirdly, in patients with combined aortic and mitral regurgitation, the volume measurement by cross sectional echocardiography still gives the total stroke volume, whereas the aortic volumetric flow measurement by Doppler technique gives only a part of it. Finally, the difference between the left ventricular total stroke volume and the transmitral volumetric flow equals the aortic regurgitant volume, whether aortic regurgitation is isolated or associated with other valvar regurgitation. If the left ventricular total stroke volume is related to the transpulmonary[24] or transtricuspid[25] volumetric flow, the aortic regurgitant volume can be calculated only in isolated aortic regurgitation.

Radionuclide ventriculography has been accepted as a reliable technique for measuring aortic regurgitation.[26-28] The good agreement between regurgitant fractions determined by Doppler and radionuclide techniques in patients with isolated aortic regurgitation indicates that our Doppler echocardiographic method is as reliable as radionuclide ventriculography in the non-invasive measurement of aortic regurgitation. The major discrepancies between the two techniques were found in patients with combined aortic and mitral regurgitation or a low left ventricular ejection fraction ($<35\%$). This is due to the fact that the radionuclide technique calculates the regurgitant volume as the difference between the left and right ventricular stroke volume, while our Doppler method calculates it as the difference between the left ventricular total stroke volume and the transmitral volumetric flow. Thus in patients with combined aortic and mitral regurgitation, the regurgitant fraction by the radionuclide technique is the sum of both aortic and mitral regurgitant fractions,[26] while our method still gives the real aortic regurgitant fraction. In one of these cases, however, a small concomitant degree of tricuspid regurgitation may have been a potential source of error in determination of the regurgitant fraction by the radionuclide technique.[26] Another major limitation of the radionuclide technique is the inaccuracy in determining the regurgitant fraction in patients with a low left ventricular ejection fraction.[29] Doppler echocardiography is probably more accurate than radionuclide techniques for measuring aortic regurgitation in patients with concomitant mitral regurgitation or impaired left ventricular function.

There are two major limitations to our method. It is difficult to measure transmitral volumetric flow when a mitral flow is disturbed, as in mitral stenosis or pronounced mitral valve fluttering. Similarly, measurement of left ventricular total stroke volume measurement is subject to errors in cases with concomitant left ventricular regional wall dyskinesia. Despite these limitations our Doppler echocardiographic method offers a new and promising approach to the non-invasive measurement of aortic regurgitation.

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